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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,682	08/27/2001	David E. Townsend	150026.464	4343

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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/940,682	TOWNSEND, DAVID E.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 10-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

Applicant's Request for Continued Examination filed 8 December 2005 has been received and entered into the case. Claim 1 has been amended. Claims 1-7 and 10-16 remain pending. All arguments have been fully considered.

Priority

Acknowledgement is made of applicant's claim for priority to provisional application 60/228,956, filed 28 August 2000, priority under 119(e) is granted.

Applicant's claim for the benefit as a CIP of prior-filed application US 08/484,593 (now US Patent 6,387,650) under 35 U.S.C. 120 is also acknowledged. However, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 08/484,593, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, the current application claims a composition comprising a conditionally detectable marker, wherein the marker is an aminopeptidase substrate comprising a signal moiety. Claim 7 requires the conditionally detectable marker to be detectable by a change in color, produced by the biochemical reduction of tetrazolium red. While 08/484,593 discloses a composition that

comprises a substrate comprising a signal moiety linked to the substrate, wherein the signal moiety can be cleaved to produce a detectable signal, it does not teach or suggest inclusion of a conditionally detectable marker that is tetrazolium red; therefore without tetrazolium red, the change in color cannot be produced by the biochemical reduction of tetrazolium red. Thus the subject matter of claim 7 is not disclosed in the parent application; however, the subject matter of claim 7 is disclosed in provisional application 60/228,956, and as such, the effective filing date of the subject matter of claim 7 is determined to be 28 August 2000. The effective filing date of the subject matter of claims 1-6 and 10-16 is determined to be 7 June 1995.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 10-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant claims a composition for detecting a target microorganism, the composition comprising a conditionally detectable marker that is a substrate for an aminopeptidase that is substantially absent from a target microorganism; wherein the substrate comprises a signal moiety linked to the substrate that provides a detectable signal when cleaved by substantially all non-target microorganisms. The target microorganism is a bacteria, yeast, mold, fungi, protozoa or virus, specifically bacteria selected from Salmonella, Listeria, E.coli OH157, Campylobacter, Staphylococcus aereus, Cryptosporidium or Giardia. The preferred bacteria are Campylobacter. The conditionally detectable marker is detectable by a color change, wherein the change in color is produced by a biochemical reduction of tetrazolium red. The enzyme is specifically L-alanine aminopeptidase; and the substrate is selected from a disclosed group,

specifically L-alanin-7-amido-4-methylcoumarin. The non-target microorganisms are substantially all non-Campylobacter species. The composition further comprises a growth supporting medium for target microorganisms, which contains all necessary nutrients and growth conditions to support target organisms.

In applicant's claim 1 the preamble is not commensurate in scope with the body of the claim. The preamble states the composition detects *target* microorganisms in a sample; however, the body of the claim teaches that *non-target* microorganism are responsible for producing the detectable signal, not the target microorganisms. Therefore it appears the composition functions to detect *non-target* microorganisms in a sample; the language of the claim must be revised to make it clear that the microorganism that cleaves the signal moiety from the substrate to produce the detectable signal is the microorganism which is detected by the composition. All dependent claims which reference the *target* or *non-target* microorganisms are further unclear because it is not clear if they are the desired "*target*" microorganisms, or if they are the contaminating "*non-target*" microorganisms that cleave the substrate to release the detectable signal.

It is further unclear in claim 1 if the signal moiety is an integral part of the substrate or if the signal moiety is linked to the substrate, and thus is not actually part of the substrate. This confusion arises from the ambiguous language, "...wherein said substrate *comprises* a signal moiety *linked to* the substrate..."

Still further, claim 1 is unclear if the conditionally detectable marker is the substrate, per se, or if the conditionally detectable marker is the signal moiety which is linked to (or part of) the substrate. Presently the claim effectively requires the conditionally detectable marker to be a substrate which comprises a detectable signal moiety; if the signal moiety is the detectable marker, it is not clear what role the substrate plays. The claim appears to be circular in construction.

Still further in claim 1 it is unclear from the phrase "wherein said marker is a substrate for an aminopeptidase that is substantially absent from the target microorganism" if it is the substrate or the aminopeptidase that is absent from the target microorganism.

Still further, the term "substantially" renders the claim indefinite, whether it refers to the level of aminopeptidase or the level of aminopeptidase substrate. The term "substantially absent" is a relative term of degree and is not defined by the claim, nor does the specification provide a standard for ascertaining the threshold limit of aminopeptidase or aminopeptidase substrate that is acceptable, yet satisfies the requirement of "substantially absent," thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Therefore the claim is rendered indefinite because one skilled in the art cannot determine the metes and bounds of the claimed subject matter.

In claim 7 it is unclear how tetrazolium red is related to the conditionally detectable marker of claim 1, it is not clear if the tetrazolium red is the signal moiety or if it is the substrate (marker). If tetrazolium red is not the signal moiety, it is unclear what is responsible for the detectable change, as claim 1 requires the signal moiety to provide the detectable signal upon cleavage, but claim 7 requires the biochemical reduction of tetrazolium red to produce the detectable color change. As such, the metes and bounds of claim 7, and in particular the structural relationship between tetrazolium red and the conditionally detectable marker, cannot be determined.

Applicant's claim 13 is rejected as being dependent upon a cancelled base claim (8); therefore the scope of claim 13 cannot be envisioned.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 10-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Carr et al (US Patent 5,064,756).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising a conditionally detectable marker that is a substrate for an aminopeptidase; wherein the substrate comprises a signal moiety linked to the substrate that provides a detectable signal when cleaved. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 14 and 15 require the composition to further comprise a growth supporting medium for target microorganisms, which contains all necessary nutrients and growth conditions to support target organisms. Claim 16 requires the composition of 14 to further comprise antibiotics. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect.

With regards to claims 2-5 and 13, which are related to the intended use of the composition (detection of specific microorganisms), please note that in cases where the body of the claim fully and intrinsically sets forth all the limitations of the invention, such as all components of a composition, recitations that merely states the intended use of the composition, rather than any distinct definition of any of the claimed invention's limitations, are not considered limitations and are of no significance to claim construction. See MPEP § 2111.02. Therefore, claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition.

Carr et al teaches a kit for antibiotic sensitivity testing, comprising a prepared microtitre plate which contains active materials for promoting growth of the microbe sample (which applicant calls a

growth supporting medium which comprises all necessary nutrients and growth conditions to properly support growth of microorganisms), antibiotics, and one or more fluorogens (See Carr et al, col. 5, ln 7-24 & col. 6, ln 4-16). As the fluorogen, Carr et al uses the hydrolysable derivatives of 4-methylcoumarin, particularly 7-N-(alanyl)-7-amido-4-methylcoumarin, which produce a detectable change in color upon cleavage by an aminopeptidase (See Carr et al, col. 4, ln 36-50, col. 6, ln 17-26 & claims). Therefore, in their kit for antibiotic sensitivity testing, Carr et al includes microtitre plates comprising growth substrate containing appropriate nutrients and materials for supporting growth of the non-target microorganisms (non-contaminating microbes), antibiotics, and the fluorogenic L-alanine-aminopeptidase substrate 7-N-(alanyl)-7-amido-4-methylcoumarin (Claims 1-6 and 10-16); therefore the reference anticipates the claimed subject matter.

Claims 1-6 and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Manafi et al (J. Applied Bacteriology, 1990).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising a conditionally detectable marker that is a substrate for an aminopeptidase; wherein the substrate comprises a signal moiety linked to the substrate that provides a detectable signal when cleaved. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect.

With regards to claims 2-5 and 13, which are related to the intended use of the composition (detection of specific microorganisms), please note that in cases where the body of the claim fully and

intrinsically sets forth all the limitations of the invention, such as all components of a composition, recitations that merely states the intended use of the composition, rather than any distinct definition of any of the claimed invention's limitations, are not considered limitations and are of no significance to claim construction. See MPEP § 2111.02. Therefore, claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition.

Manafi et al teach a composition comprising the conditionally detectable marker L-alanine-7-amido-4-methylcoumarin (AAMC), which produces a fluorescent color change when cleaved by the L-alanine-aminopeptidase found in the cell wall of Gram-negative bacteria (See Manafi et al, See pages 823-827) (Claims 1-6 and 10-13). Therefore the reference anticipates the claimed subject matter.

Claims 1-7 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Tuompo et al (US Patent 5,420,017).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising a conditionally detectable marker that is a substrate for an aminopeptidase; wherein the substrate comprises a signal moiety linked to the substrate that provides a detectable signal when cleaved. Claim 6 requires the conditionally detectable marker to be detectable by a color change; claim 7 requires the change in color to be produced by a biochemical reduction of tetrazolium red. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect.

With regards to claims 2-5 and 13, which are related to the intended use of the composition (detection of specific microorganisms), please note that in cases where the body of the claim fully and intrinsically sets forth all the limitations of the invention, such as all components of a composition, recitations that merely states the intended use of the composition, rather than any distinct definition of any

of the claimed invention's limitations, are not considered limitations and are of no significance to claim construction. See MPEP § 2111.02. Therefore, claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition.

Tuompo et al teach a composition for detecting the presence of Gram-negative bacteria, wherein the composition comprises a test solution comprising a chromogenic reagent in an amount effective to detect the Gram negative bacteria; preferably the chromogenic reagent is a tetrazolium salt, particularly triphenyltetrazolium chloride (tetrazolium red), which produces a color change from colorless to red upon biochemical reduction (which applicant calls a conditionally detectable marker comprising a signal moiety). Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al (US Patent 5,064,756).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising a conditionally detectable marker that is a substrate for an aminopeptidase; wherein the substrate comprises a signal moiety linked to the substrate that provides a detectable signal when cleaved. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 14 and 15 require the composition to further comprise a growth supporting medium for target

microorganisms, which contains all necessary nutrients and growth conditions to support target organisms. Claim 16 requires the composition of 14 to further comprise antibiotics. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect; however claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition, see above.

Carr et al teaches a kit for antibiotic sensitivity testing, comprising a prepared microtitre plate which contains active materials for promoting growth of the microbe sample (which applicant calls a growth supporting medium which comprises all necessary nutrients and growth conditions to properly support growth of microorganisms), antibiotics, and one or more fluorogens (See Carr et al, col. 5, ln 7-24 & col. 6, ln 4-16). As the fluorogen, Carr et al uses the hydrolysable derivatives of 4-methylcoumarin, particularly 7-N-(alanyl)-7-amido-4-methylcoumarin, which produce a detectable change in color upon cleavage by an aminopeptidase (See Carr et al, col. 4, ln 36-50, col. 6, ln 17-26 & claims).

While Carr et al does teach that derivatives of 4-methylcoumarin can be used in their invention, they do not teach the specific amino acid-containing derivatives that are presently claimed. However, it would have been well within the purview of one of ordinary skill in the art, at the time the invention was made, to use any of the well known amino acid-containing derivatives of 4-methyl-coumarin, including L-alanine-7-amido-4-methylcoumarin TFA, L-alanine-7-amido-4-trifluoro-methylcoumarin TFA, L-alanyl-L-alanyl-L-phenylalanine-7-amido-4-methylcoumarin, and L-alanyl-L-alanyl-L-phenylalanine-7-amido-4-methylcoumarin TFA. One would have been motivated to use any of the well known derivatives and would have expected success because the prior art teaches the detectable change in fluorescence is due to the cleavage of the peptide bond, which releases the methylcoumarin fluorogen; attachment of any amino acid residue to the amido methylcoumarin would present the appropriate bond for cleavage. Furthermore, Carr et al exemplify -N-(alanyl)-7-amido-4-methylcoumarin as the substrate, which is

cleaved by an L-alanine aminopeptidase; therefore, one of ordinary skill in the art would have been motivated to use other L-alanine aminopeptidase substrates, such as those listed above, as they are functional equivalents for testing the presence of L-alanine aminopeptidase. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-6 and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manafi et al (J Applied Bacteriology, 1990).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising a conditionally detectable marker that is a substrate for an aminopeptidase; wherein the substrate comprises a signal moiety linked to the substrate that provides a detectable signal when cleaved. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 14 and 15 require the composition to further comprise a growth supporting medium for target microorganisms, which contains all necessary nutrients and growth conditions to support target organisms. Claim 16 requires the composition of 14 to further comprise antibiotics. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect; however claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition, see above.

Manafi et al teach a composition comprising the conditionally detectable marker L-alanine-7-amido-4-methylcoumarin (AAMC), which produces a fluorescent color change when cleaved by the L-

alanine-aminopeptidase found in the cell wall of Gram-negative bacteria (See Manafi et al, See pages 823-827).

Manafi et al exemplify L-alanine-7-amido-4-methylcoumarin as the substrate, which is cleaved by an L-alanine aminopeptidase; therefore, while they do not teach other derivatives of L-alanine-7-amido-methylcoumarin, it would be within the purview of one of ordinary skill in the art to select other functionally equivalent substrates, including L-alanine-7-amido-4-methylcoumarin TFA, L-alanine-7-amido-4-trifluoro-methylcoumarin TFA, L-alanyl-L-alanyl-L-phenylalanine-7-amido-4-methylcoumarin, and L-alanyl-L-alanyl-L-phenylalanine-7-amido-4-methylcoumarin TFA. It is known that the L-alanine aminopeptidase will cleave the substrate at the L-alanine residue to release the amido-methylcoumarin fluorogen, substitution of different substrates that comprise the same L-alanine-7-amido-4-methylcoumarin core would be expected to function equivalently, especially in absence of evidence to the contrary. Therefore, one of ordinary skill in the art would be motivated to use the derivatives of L-alanine-7-amido-4-methylcoumarin listed above as alternatives to the substrate of Manafi et al, and would expect success in doing so, based on the fact that the functional core structure remains unchanged, and thus the derivatives would be considered functional equivalents. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 8 December 2005 have been fully considered. Due to the amendment to claim 1, claims 1-6 and 10-16 are now found to be fully supported by the parent application 08/484,593 filed 7 June 2005, claims 1-7 and 10-16 are found to be fully supported by provisional application 60/228,956 filed 28 August 2000, as noted above. Due to the new effective filing

date considerations, the rejections involving Townsend (WO 96/40980) have been withdrawn; however, new rejections, as set forth above, have been made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651